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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,894	04/14/2006	Katsuyuki Hamada	TSU-007	4681

38051 7590 04/01/2009

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EXAMINER
SHEN, WU CHENG WINSTON

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
04/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,894	HAMADA ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *4-7 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response received on 01/04/2009 has been entered. Claims 1-10 are pending. Claims 1-10 are amended.

Claims 4-7 and 9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-3, 8 and 10 are currently under examination to the extent of elected species A549 cell (claim 1), 1A1.3B promoter (claim 2), and adenovirus (claims 3 and 10).

This application 10/575,894 is a 371 of PCT/JP04/15221 filed on 10/15/2004, which claims the priority of JAPAN 2003-354983, filed on 10/15/2003.

Priority

1. The following statement has been documented on page 3 of the office action mailed on 09/04/2009.

This application 10/575,894 filed on 04/14/2006, the filed Oath and Declaration filed on 04/14/2006 claims benefit of foreign application Japan 2003-354983 filed on 10/15/2003. The Examiner acknowledges that Applicant has submitted on 04/14/2006 a certified copy of Japan 2003-354983 filed on 10/15/2003 under requirement of 35 U.S.C. 119 (a-d) conditions. However, it is noted that, the application Japan 2003-354983 filed on 10/15/2003 is in Japanese. Therefore, without a certified translation of Japan 2003-354983 filed on 10/15/2003, the effective filing date for the instant claims is the filing date of PCT/JP04/15521, 10/15/2004.

Applicant cannot rely upon the foreign priority papers to overcome the rejection under 35 USC 102 (e) or 102 (a) as set forth below because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Objections

2. Previous objection of claims 1-3, 8, and 10 for recitation of the term "a cancer gene therapeutic drug", is ***withdrawn*** because the term has been amended to read as "a composition comprising a carrier cell for gene therapy in treating cancer".

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Applicant's arguments pertaining to 102 rejections and Examiner's ***Response to Applicant's arguments*** are addressed collectively at the end of three 102 rejections documented below.

3. Claims 1-3, and 10 remain rejected under 35 U.S.C. 102(b) as being anticipated by **Hamada et al.** (Hamada et al., Identification of the human IAI.3B promoter element and its use in the construction of a replication-selective adenovirus for ovarian cancer therapy. *Cancer Res.* 63(10):2506-12, 2003; this reference is listed citation #1 on the IDS filed on 07/06/2008). Applicant's arguments filed 01/04/2008 have been fully considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on pages 4-5 of the office action mailed on 09/04/2008.

For clarity of this office action, the rejection for the reasons of record advanced on pages 4-5 of the office action mailed on 09/04/2008 is reiterated below, with revision addressing claim amendments filed on 01/04/2009.

Claim interpretation: The phrase "for gene therapy in treating cancer" recited in the preamble of claims 1-3 and 10 is the intended use of the composition and considered for limited patentable weight, if any. The intended use "for immunological treatment" recited in line 2 of claims 3 and 10 are considered for limited patentable weight, if any. It is the claimed composition that imparts patentable weight for prior art rejection.

Hamada et al. disclosed the following teachings : **(i)** Identification of the promoter region of the IAI.3B gene and construction of a replication-selective adenovirus, AdE3-*IAI.3B*, driven by the promoter (See abstract and Figure 2, Hamada et al., 2003); **(ii)** The lung cancer A549 transfected with an oncolytic adenovirus Ad*E2F-1*^{RC}, and AdE3-*IAI.3B* has a construction design similar to that of the adenovirus Ad*E2F-1*^{RC}, because both have an intact *E1A* promoter upstream of their respective heterologous promoters (See Discussion, second paragraph, right column, page 2510, Hamada, 2003), and **(iii)** AdE3-*IAI.3B* replicated as efficiently as the wild-type adenovirus and caused extensive cell killing in a panel of ovarian cancer cells *in vitro*, in contrast, squamous cell carcinoma and normal cells were not able to support AdE3-*IAI.3B* replication (See abstract and Figure 3, Hamada et al., 2003), and **(iv)** In animal studies, AdE3-*IAI.3B* administered to flank and i.p. xenografts of ovarian cancer cells led to a significant therapeutic effect (See abstract and Figure 4, Hamada et al., 2003).

Thus, Hamada et al. (2003) clearly anticipates the claims 1-3 and 10 of instant invention.

4. Claims 1, 3, and 10 remain rejected under 35 U.S.C. 102(b) as being anticipated by **Tsukuda et al.** (Tsukuda et al., An E2F-responsive replication-selective adenovirus targeted to the defective cell cycle in cancer cells: potent antitumoral efficacy but no toxicity to normal cell.

Cancer Res. 62(12):3438-47, 2002; this reference is listed citation #5 on the IDS filed on 07/06/2008). Applicant's arguments filed 01/04/2008 have been fully considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on pages 5-6 of the office action mailed on 09/04/2008.

For clarity of this office action, the rejection for the reasons of record advanced on pages 5-6 of the office action mailed on 09/04/2008 is reiterated below, with revision addressing claim amendments filed on 01/04/2009.

Claim interpretation: The phrase "for gene therapy in treating cancer" recited in the preamble of claims 1-3 and 10 is the intended use of the composition and considered for limited patentable weight, if any. The intended use "for immunological treatment" recited in line 2 of claims 3 and 10 are considered for limited patentable weight, if any. It is the claimed composition that imparts patentable weight for prior art rejection.

Tsukuda et al. disclosed the following teachings : (i) The construction of an adenovirus Ad*E2F-1*^{RC} and transfection of the Ad*E2F-1*^{RC} in A549 cells, so that E1A expression and viral replication were under the control of the human E2F-1 promoter element (See abstract and Material and Methods, left column, page 3440, Tsukuda et al., 2002); (ii) The Ad*E2F-1*^{RC} virus replicated as efficiently as the wild-type adenovirus and caused extensive cell killing in a panel of tumor cells (i.e. an oncolytic virus) *in vitro*, in contrast, non-proliferating normal epithelial, fibroblast,

and endothelial cells, which express no E2F-1, were not able to support Ad*E2F-1*^{RC} replication (See abstract and Figures 3-5, Tsukuda et al., 2002); and **(iii)** In animal studies, different dosing regimens of Ad*E2F-1*^{RC} administered to flank xenografts of ovarian and lung cancers led to a significant therapeutic advantage often surpassing that seen in animals treated with the wild-type adenovirus (See abstract and Figures 6-7, Tsukuda et al., 2002).

Thus, Tsukuda et al. (2002) clearly anticipates the claims 1, 3, and 10 of instant invention.

5. Claims 1, 3, and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by **Li et al.** (US Patent 7,026,164, issued Apr. 11, 2006, file don 07/03/2003). Previous rejection is ***maintained*** for the reasons of record advanced on pages 6-7 of the office action mailed on 09/04/2008.

For clarity of this office action, the rejection for the reasons of record advanced on pages 6-7 of the office action mailed on 09/04/2008 is reiterated below, with revision addressing claim amendments filed on 01/04/2009.

Claim interpretation: The phrase "for gene therapy in treating cancer" recited in the preamble of claims 1-3 and 10 is the intended use of the composition and considered for limited patentable weight, if any. The intended use "for immunological treatment" recited in line 2 of claims 3 and 10 are considered for

limited patentable weight, if any. It is the claimed composition that imparts patentable weight for prior art rejection.

Li et al. teaches adenovirus packing cell lines and the infection of 4 different oncolytic adenovirus (CG8900, CG8840, OV945 and OV1025) to A549 cell line, a lung cancer cell line (See abstract, bridging paragraph, columns 19-20, and Table 2, Li et al., 2006).

Thus, Li et al. (2006) clearly anticipates the claims 1, 3, and 10 of instant invention.

Applicant's arguments

Applicant argues that the composition of the present invention can achieve excellent anti-tumor effects both in vitro and in vivo. Applicant argues that the cited reference the cited references - Hamada 2003, Tsukuda 2002 & Li '164 - do not mention the use of carrier cells. These references only teach that PA-1 cells and A549 cells can be used for oncogenesis, virus production or virus proliferation. Applicant argues that these references do not specifically teach the use of the disclosed cells as carrier cells. Applicant argues that the use of these specific cells as "carrier cells" is an important aspect of the claims and therefore, the failure to disclose the use of these specifically claimed cells as "carrier cells" in the cited references show they do not anticipate claims 1, 3 and 10.

Response to Applicant's arguments

The Hamada 2003, Tsukuda 2002 & Li '164 references do teach A549 cell (which Applicant calls "a carrier cell" in recited composition) transfected with oncolytic adenovirus, wherein the adenovirus comprises a 1A1.3B promoter. Accordingly, the cited references do disclose all the limitations in the claimed composition.

The intended use and inherent properties are not considered with patentable weight for the claimed composition because the components of the composition remain the same. Intended used does not impart patentable weight to a product. See MPEP 2111.03:

> Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey 370 F.2d 576, 152 USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459, (CCPA 1963).

See also, MPEP 2111.02(II) also, which recites, "If a prior art structure is capable of performing the intended use as recited in the preamble, then it meets the claim. See, e.g., In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997)" and 2112-2112.01. See also Catalina Mktg. Int 'l v. Coolsavings.com, Inc., 289 F.3d at 808-09, 62 USPQ2d at 1785 ("[C]lear reliance on the preamble

during prosecution to distinguish the claimed invention from the prior art transforms the preamble into a claim limitation because such reliance indicates use of the preamble to define, in part, the claimed invention....Without such reliance, however, a preamble generally is not limiting when the claim body describes a structurally complete invention such that deletion of the preamble phrase does not affect the structure or steps of the claimed invention." This is the case here, since the preamble "for gene therapy in treating cancer" does not affect the structure of the claimed product.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1 and 8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over **Tsukuda et al.** (Tsukuda et al., An E2F-responsive replication-selective adenovirus targeted to the defective cell cycle in cancer cells: potent antitumoral efficacy but no toxicity to normal cell.

Cancer Res. 62(12):3438-47, 2002; this reference is listed citation #5 on the IDS filed on 07/06/2008) in view of **Molnar-Kimber et al.** (Molnar-Kimber et al., WO 99/45783, international publication date, 09/16/1999; this reference is listed on the IDS filed

on 03/26/2007). Previous rejection is ***maintained*** for the reasons of record advanced on pages 7-10 of the office action mailed on 09/04/2008.

For clarity of this office action, the rejection for the reasons of record advanced on pages 7-10 of the office action mailed on 09/04/2008 is reiterated below, with revision addressing claim amendments filed on 01/04/2009.

Claim interpretation: The phrase "for gene therapy in treating cancer" recited in the preamble of claims 1 and 8 is the intended use of the composition and considered for limited patentable weight, if any. It is the claimed composition that imparts patentable weight for prior art rejection.

Tsukuda et al. disclosed the following teachings : (i) The construction of an adenovirus Ad*E2F-1*^{RC} and transfection of the Ad*E2F-1*^{RC} in A549 cells, so that E1A expression and viral replication were under the control of the human E2F-1 promoter element (See abstract and Material and Methods, left column, page 3440, Tsukuda et al., 2002); (ii) The Ad*E2F-1*^{RC} virus replicated as efficiently as the wild-type adenovirus and caused extensive cell killing in a panel of tumor cells (i.e. an oncolytic virus) *in vitro*, in contrast, non-proliferating normal epithelial, fibroblast, and endothelial cells, which express no E2F-1, were not able to support Ad*E2F-1*^{RC} replication (See abstract and Figures 3-5, Tsukuda et al., 2002); and (iii) In animal studies, different dosing regimens of Ad*E2F-1*^{RC} administered to flank xenografts of ovarian and lung cancers led to a significant therapeutic advantage often

surpassing that seen in animals treated with the wild-type adenovirus (See abstract and Figures 6-7, Tsukuda et al., 2002).

Tsukuda et al. do not teach the limitation "furthering comprising a tumor cell to be administered for tumor vaccination" as recited in claim 8 of instant application.

However, Molnar-Kimber et al. teaches the following: (i) A producer cell (i.e. a tumor cell line for viral packaging) comprises an oncolytic adenovirus which is capable of replicating in the producer cell and methods of using these producer cells to treat a subject having tumor cells and making a medicament for use in such treatment (See abstract, third paragraph, page 7, Molnar-Kimber et al., WO 99/45783) , and (ii) A producer cell (i.e. a tumor cell line for viral packaging) may also be rendered incapable of sustained survival in the body of the patient by exposing the producer cell to a lethal dose of radiation prior to providing the producer cell to the subject, and formation of a producer cell-tumor cell complex may generate or expose antigenic regions which can be recognized by the subject's immune system, leading to generation of an immune response against the tumor cells (See lines 5-8, 28-30, page 13, Molnar-Kimber et al., WO 99/45783).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Tsukuda et al. regarding administration of A459 cells infected with oncolytic adnovirus Ad*E2F-1*^{RC} to animals for cancer treatment with the teachings of Molnar-Kimber et al.

regarding a radiated producer cell (i.e. a tumor cell line for viral packaging) infected with oncolytic adenovirus forming a complex with tumor cell complex that can leads to generation of an immune response against the tumor cells, to arrive at a composition including A549 cell infected with an oncolytic adenovirus and further comprising a tumor cell to be administered for tumor vaccination, as recited in claim 8 of instant application.

One having ordinary skill in the art would have been motivated to combine the teachings of Tsukuda et al. and Molnar-Kimber et al. because there are two different molecular mechanisms involved in treating cancer by a producer/packing cell line infected with an oncolytic adenovirus. The administration of non-radiated A459 cells infected with mutated oncolytic adenovirus Ad*E2F-1*^{RC} taught by Tsukuda et al. results to killing of cancer cells, and the administration of radiated producer cell (i.e. a tumor cell line for viral packaging) infected with oncolytic adenovirus forming a complex with tumor cell complex, taught by Molnar-Kimber et al., can generate an immune response against the tumor cells.

There would have been a reasonable expectation of success given (i) successful demonstration of treating cancer cells A459 cells infected with replication-selective oncolytic adenovirus Ad*E2F-1*^{RC} leads to potent anti-tumoral efficacy but no toxicity to normal cells by the teachings of Tsukuda et al. and (ii) the immune response against cancer cells elicited by the administration of radiated

producer cell infected with oncolytic adenovirus by the teachings of Molnar-Kimber et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Applicant's arguments

Applicant argues that neither Tsukuda 2002 nor Molnar-Kimber '783 mentions the use of A549, SW626 and HT-3 as carrier cells. Applicant argues that it appears that the importance of these specific carrier cells has been overlooked during examination. Applicant argues that in the composition comprising a carrier cell for gene therapy in treating cancer of the present invention, specific carrier cells are identified as suitable for use as carrier cells in the present application, and these cells achieve significantly stronger anti-tumor effects with the use of oncolytic viruses in the treatment of tumors. The references cited in the Office Action do not teach or suggest the specific features and effects of the present invention. Applicant argues that, as mentioned above, an important feature of the present invention is the use of these specific cells as "carrier cells". Applicant argues that the failure to disclose the use of these specifically claimed cells as "carrier cells" in the cited references show they do not individually, or in combination, disclose, each and every feature, of Claims 1 and 8.

Response to Applicant's arguments

The Tsukuda 2002 reference does teach A549 cell (which Applicant calls "a carrier cell" in recited composition) transfected with oncolytic adenovirus. Accordingly, the cited reference does disclose all the limitations of the composition of claim 1 because there is no evidence on the record the structure of A549 cell taught by Tsukuda 2002 is any different from the structure of claimed A549 cell.

The intended use and inherent properties are not considered with patentable weight for the claimed composition because the components of the composition remain the same. Intended used does not impart patentable weight to a product. See MPEP 2111.03:

> Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey 370 F.2d 576, 152 USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459, (CCPA 1963).

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by

telephone are unsuccessful, the supervisory patent examiner, Peter Paras, Jr. can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wu-Cheng Winston Shen/
Patent Examiner
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